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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,280	01/24/2005	Michael J Caulfield	20930P	8769
210 7590 12/18/2007 MERCK AND CO., INC P O BOX 2000 RAHWAY, NJ 07065-0907			EXAMINER BARNHART, LORA ELIZABETH	
			ART UNIT 1651	PAPER NUMBER
			MAIL DATE 12/18/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/522,280	Applicant(s) CAULFIELD ET AL.	
	Examiner Lora E. Barnhart	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 21-63 is/are pending in the application.
- 4a) Of the above claim(s) 3,4,21,22,24 and 27-63 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,23,25 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendments

Applicant's amendments filed 10/1/07 to the claim listing has been entered. Claims 5-20 have been cancelled. No claims have been amended or added. Claims 1-4 and 21-63 remain pending in the current application, of which claims 1, 2, 23, 25, and 26 ONLY are being considered on their merits. Claims 3, 4, 21, 22, 24, and 27-63 remain withdrawn from consideration at this time. Prior art references not included with this Office action can be found in a prior action.

Specification

The objections to the specification are withdrawn in light of the amendments to the specification and the new abstract.

Claim Objections

The objection to the claims is withdrawn. However, all future claim listings should comprise lines one and one-half or, preferably, double spaced. See 37 CFR 1.52(b).

Claim Rejections - 35 USC § 112

The rejections of record under 35 U.S.C. § 112, second paragraph, are rendered moot by the cancellation of the relevant claims.

Claim Rejections - 35 USC § 103

Any obviousness rejections of record not particularly addressed below are rendered moot by the cancellation of claims 5-20.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 23, 25, and 26 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Minnich et al. (2002, U.S. Patent 6,365,368; on 5/19/05 IDS) taken in view of Lehmann et al. (2002, U.S. Patent 6,410,252).

Minnich teaches a method for counting *E. coli* colonies comprising transferring liquid cultures containing various numbers of microbes to the wells of a 96-well nitrocellulose filter plate (column 6, lines 37-47); removing the culture media using suction filtration through the nitrocellulose filter, thus immobilizing the microbes on the filter (column 6, lines 49-51); adding a nonselective medium to each well and allowing the microbes to grow for 12 hours (column 6, lines 52-56); and assaying the presence of microbes using antibodies specific to said microbes (column 6, lines 58-67).

Minnich does not teach counting colonies of microbes on the filter plate. Minnich does not teach culturing the microbes on the filter plate for the time required in claim 7. Minnich does not exemplify a method for counting Gram-positive bacteria as required in claim 23, e.g. *S. pneumoniae* as in claim 26.

Lehmann teaches a method of detecting, categorizing, and counting spots on a membrane comprising treating each filter (membrane) in a multiwell filter plate such that spots develop; capturing an image of each well in the plate; digitizing the images; and thresholding said images such that spots are detected, categorized, and counted (column 4, lines 40-54). Lehmann teaches that the step of treating the filter such that spots develop may comprise adding living cells to the well (column 3, lines 23-37). The plate of Lehmann is preferably a 96-well plate with a membrane at the bottom of each well (column 7, lines 50-53; Figure 1). While the working examples of Lehmann are drawn to monitoring T cell responses, Lehmann contemplates that the method may be used to assay suspensions of other biological materials (column 8, lines 10-12).

A person of ordinary skill in the art would have had a reasonable expectation of success in substituting the spot counting step of Lehmann for the immunological detection step of Minnich because Minnich's method is a method for determining whether water has microbe contamination, so counting and identifying colonies of microbes within a sample is a functional equivalent for a positive result in an immunological assay designed to detect microbes. The skilled artisan would have further expected success in using the method of Lehmann to count any kind of bacterial colonies (including Gram-positive bacteria such as *S. pneumoniae*) because Lehmann specifically teaches that the method may be used to enumerate spots of any kind, including suspensions of cells. The skilled artisan would have been motivated to substitute the counting step of Lehmann for the immunological assay of Minnich

because the counting step does not necessarily destroy the cells, as the immunological assay step does, so the contaminating microbes could be preserved for further study.

The person of ordinary skill in the art would have had a further reasonable expectation of success in using the method of Minnich in which the counting step of Lehmann has been substituted for the immunological assay step to enumerate Gram-positive bacteria, e.g. *S. pneumoniae*, because Lehmann teaches that the counting method has broad application to suspensions of all cells. The selection of type of bacteria to count using such a method would therefore have been a routine matter of optimization on the part of the artisan of ordinary skill. A holding of obviousness over the cited claims is therefore clearly required.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to assay for any bacteria using the method of Minnich in which the counting step of Lehmann has been substituted for the immunological assay step because the counting step and the immunological assay step provide similar information in terms of water contamination, and because the counting step may be applied to any cells.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Applicant alleges, "it would be unlikely for a person of ordinary skill in the art to combine the teaching of [Minnich] with the teaching of Lehmann" (Reply, page 11, first full paragraph). Applicant alleges that the cited prior art does not teach or suggest all of the claim elements (*ibid.*). Applicant alleges that the rejection does not meet the

standard set forth by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007) (*ibid.*). These arguments have been fully considered, but they are not persuasive.

The Minnich reference teaches or exemplifies every element of the claims except for the quantitative counting step. It is this aspect of the Lehmann reference that is relied upon in the rejection of record. It is not disputed that Minnich does not teach counting colonies, but Minnich does teach a step in which the bacteria on the filter plate are quantified by contacting them with labeled antibodies and assaying the degree of color change (see column 6, line 58, through column 7, line 13, e.g.), and Lehmann teaches that cell colonies contacted with labeled antibodies may be counted. It would have been obvious to substitute the counting step of Lehmann for the color assay step of Minnich.

The portion of the decision in *KSR* cited by applicant may be found at page 14 of the *KSR* decision in the first paragraph after section heading B, in a discussion of the analysis advocated by the CCPA. Identifying a motivation to combine references in an obviousness rejection may constitute a "helpful insight," but the Court writes, "The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents" (see *KSR* at 15). The *KSR* decision advocates the use of common sense in identifying the difference between true innovation and routine experimentation that would be within the purview of the person of ordinary skill in the art, who is "also a person of ordinary creativity, not an automaton"

(see *KSR* at 17). As taught by Lehmann, counting colonies of cells grown on a membrane was known in the art at the time of the invention for determining the presence of cells and enumerating them. The cited prior art, taken together and in light of the art as a whole at the time of the invention, renders the instant invention obvious.

Claims 1, 2, 23, 25, and 26 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al. (2001, WO01/059157; on 5/19/05 IDS) taken in view of Lehmann et al. (2002, U.S. Patent 6,410,252).

Young teaches a method for enumerating bacterial colonies in a liquid sample comprising adding bacteria to a filter, incubating the bacteria from 1 to 24 hours such that colonies are formed, and counting the number of colonies on said filter (pages 2, 4, and 5). Young teaches removing excess media from the filter using a vacuum (page 2). The preferred filter of Young is one with hydrophilic regions separated from each other by hydrophobic partitions (page 4). Young teaches that any microorganism can be assayed using the method (page 2) and that any manner of enumerating the colonies may be used, so long as the colonies are counted (page 5).

Young does not teach a method in which colonies are assayed in a multi-well plate.

Lehmann teaches a method of detecting, categorizing, and counting spots on a membrane comprising treating each filter (membrane) in a multiwell filter plate such that spots develop; capturing an image of each well in the plate; digitizing the images; and thresholding said images such that spots are detected, categorized, and counted

(column 4, lines 40-54). Lehmann teaches that the step of treating the filter such that spots develop may comprise adding living cells to the well (column 3, lines 23-37). The plate of Lehmann is preferably a 96-well plate with a membrane at the bottom of each well (column 7, lines 50-53; Figure 1). While the working examples of Lehmann are drawn to monitoring T cell responses, Lehmann contemplates that the method may be used to assay suspensions of other biological materials (column 8, lines 10-12).

A person of ordinary skill in the art would have had a reasonable expectation of success in substituting the 96-well plate assay of Lehmann for the single filter assay of Young because Young teaches that any membrane filter may be used in the method, so long as microorganisms can grow thereon (page 4). The skilled artisan would have been motivated to substitute the 96-well plate format of Lehmann for the single filter of Young for the expected benefit that many different samples could be evaluated in a single assay. Automating a manual activity (in this case, automating the manual examination of 96 single filters of Young by including them all in the single multiwell filter of Lehmann) is obvious. See M.P.E.P. § 2144.04.

The person of ordinary skill in the art would have had a further reasonable expectation of success in using the method of Young in which the multiwell format of Lehmann has been substituted for the immunological assay step to enumerate *S. pneumoniae* because Lehmann teaches that the counting method has broad application to suspensions of all cells and because Young teaches that any type of microorganism may be assayed using the method. The selection of type of bacteria to count using such a method would therefore have been a routine matter of optimization on the part of the

artisan of ordinary skill. A holding of obviousness over the cited claims is therefore clearly required.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to assay for any bacteria using the method of Young in which the 96-well assay format of Lehmann has been substituted for the single filter assay because more samples could be evaluated in a single assay, and because the counting step may be applied to any cells.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Applicant alleges that the cited prior art does not teach or suggest all of the claim elements (Reply, page 11, second full paragraph). Applicant alleges that the rejection does not meet the standard set forth by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007) (*ibid.*). These arguments have been fully considered, but they are not persuasive.

Applicants urge that neither of the cited references suggests the invention as claimed. The Young reference teaches or exemplifies every element of the claims except for growing cells in multi-well format. It is this aspect of the Lehmann reference that is relied upon in the rejection of record. It is not disputed that Young does not teach a multiwell plate, but Young does teach a step in which the bacteria are grown on a filter, and Lehmann teaches that cell culture vessels may be in multiwell format. It would have been obvious to substitute the multiwell format of Lehmann for the single plate of Minnich in order to screen more than one sample at once.

Applicant's basis for stating that the examiner's basis for her conclusion of obviousness is not "explicit" and that it lacks "articulated reasoning" is not clear. In the original ground of rejection (and reiterated above), the examiner indeed provided a motivation to combine the references and reasons to expect success in combining them. Applicant has provided no evidence that the assay of Young could not be carried out in multiwell format. Given the teachings of Lehmann that this format was well known in the art at the time of the invention for screening numerous samples simultaneously, carrying out the method of Minnich in multiwell format in order to make the method high-throughput would have been obvious.

No claims are allowed. No claims are free of the art.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lora E Barnhart
Examiner/Partial Signatory Authority
Temporary Full Signatory Authority (as of 12/9/07)

